PATENT
Attorney Docket No. 24512-X

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Arnold J. REUSER et al.

Serial No: 09/886,477

Filed: June 22, 2001

For: **METHODS OF PURIFYING HUMAN ACID ALPHA-GLUCOSIDASE**

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, D.C. 20231

Sir:

Before action in this application, please amend the above-identified application as follows:

IN THE CLAIMS

Please cancel claims 38-39 without any prejudice or disclaimer to the subject matter expressed therein and amend claims 3-5, 7-8, 10-11, 14, 18, 22, 24-25, 27-28, 32-35, and 37 as indicated in Appendices A and B submitted herewith. Appendix A is a marked-up copy of the amended claims and Appendix B is a clean copy of the amended claims.

REMARKS

Claims 1-37 are currently pending in the present application. The amendments do not add any new matter under 35

U.S.C. §132. Accordingly, entry of the amendments prior to examination of the application is respectfully requested.

Respectfully submitted,

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Date: November 15, 2001

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BOX PATENT
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Appendix A

Please cancel presently pending claims 38-39 and amend the following claims as indicated in the following marked up copy of the claims.

3. (Once Amended) The method of claim 2 [or claim 3], wherein the anion exchange column is Q-Ssepharose.

4. (Once Amended) The method of claim [4] 3, wherein the sample is applied to the Q-Sepharose column in low salt buffer and is eluted from the column in an elution buffer of higher salt concentration.

5. (Once Amended) The method of claim 2 [or claim 3], wherein the anion exchange column is copper chelating Sepharose.

7. (Once Amended) The method of claim 2 [or claim 3], wherein the hydrophobic interaction column is phenyl Sepharose.

8. (Once Amended) The method of claim 2 [or claim 3], wherein the hydrophobic interaction column is Source Phenyl 15.

10. (Once Amended) The method of [any one of claims] claim 2 [to 9], further comprising repeating steps (a) and (b) and/or

(c) until the a-glucosidase has been purified to 95%, preferably 99%, more preferably 99.9% w/w pure.

11. (Once Amended) The method of [any one of claims] claim 2 [to 10], wherein the sample is milk produced by a transgenic mammal expressing the a-glucosidase in its milk.

14. (Once Amended) The method of [any one of claims] claim 11 [to 13], further comprising centrifuging the milk and removing fat leaving skimmed milk.

18. (Once Amended) The method of [any preceding] claim 1, wherein the sample has a volume of at least 100 liters.

22. (Once Amended) At least 95%, preferably at least 99%, more preferably at least 99.9% w/w pure human [Human] acid a-glucosidase [of any one of claims 19-21] produced by the process of [any one of claims 1-18] claim 1.

24. (Once Amended) A pharmaceutical composition comprising human acid a-glucosidase as claimed in [any one of claims 19-21] claim 19.

25. (Once Amended) Human acid a glucosidase of [any one of claims 19-21] claim 19 for use as a pharmaceutical.

27. (Once Amended) The use of human acid a-glucosidase of [any one of claims 19-21] claim 19 for the manufacture of a medicament for treatment of human acid a-glucosidase deficiency.

28. (Once Amended) The use of human acid a-glucosidase of [any one of claims 19-21] claim 19 for the manufacture of a medicament for intravenous administration for the treatment of human acid a-glucosidase deficiency.

32. (Once Amended) A method as claimed in [any of claims]

claim 29 [to 31] being a batch procedure.

33. (Once Amended) A method as claimed in [any of claims] claim 29 [to 31], wherein the hydroxylapatite is in the form of a column, optionally the method is a liquid column chromatography procedure.

34. (Once Amended) A method as claimed in [any of claims] claim 29 [to 33], wherein the heterologous protein [ie] is selected from the group consisting of [lactoferrin, transferrin, lactalbumin, factor IX, growth hormone, a-anti-trypsin,] lactoferrin, transferrin, lactalbumin, coagulation factors such as factor VIII and factor IX, growth hormone, a-anti-trypsin, plasma proteins such as serum albumin, C1-esterase inhibitor and fibrinogen, collagen, immunoglobulins, tissue plasminogen activator, interferons, interleukins, peptide hormones, and lysosomal proteins such as a-glucosidase, a-L-iduronidase, iduronate-sulfate sulfatase, hexosaminidase A and B, ganglioside activator protein, arylsulfatase A and B, iduronate sulfatase, heparan N-sulfatase, galactoceramidase, a-galactosylceramidase A, sphingomyelinase, a-fucosidase, a-mannosidase, aspartylglycosamine amide hydrolase, acid lipase, N-acetyl-a-D-glycosamine-6-sulphate sulfatase, a-and ss-galactosidase, ss-glucuronidase, ss-mannosidase, ceramidase, galactocerebrosidase, a-N-acetylgalactosaminidase, and protective protein and others including allelic, cognate or induced variants as well as polypeptide fragments of the same.

35. (Once Amended) A method as claimed in [any of claims] claim 29 [to 24], wherein the heterologous protein is not one

normally found in the milk of an animal.

37. (Once Amended) The method of claim **[26]** 36, wherein the hydroxylapatite is in the form of a column and the unbound fraction is collected in the flow-through.

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Appendix B

Please cancel presently pending claims 38-39 and amend the following claims as indicated in the following clean copy of the claims.

3. (Once Amended) The method of claim 2, wherein the anion exchange column is Q-Ssepharose.

4. (Once Amended) The method of claim 3, wherein the sample is applied to the Q-Sepharose column in low salt buffer and is eluted from the column in an elution buffer of higher salt concentration.

5. (Once Amended) The method of claim 2, wherein the anion exchange column is copper chelating Sepharose.

7. (Once Amended) The method of claim 2, wherein the hydrophobic interaction column is phenyl Sepharose.

8. (Once Amended) The method of claim 2, wherein the hydrophobic interaction column is Source Phenyl 15.

10. (Once Amended) The method of claim 2, further comprising repeating steps (a) and (b) and/or (c) until the a-

glucosidase has been purified to 95%, preferably 99%, more preferably 99.9% w/w pure.

11. (Once Amended) The method of claim 2, wherein the sample is milk produced by a transgenic mammal expressing the a-glucosidase in its milk.

14. (Once Amended) The method of claim 11, further comprising centrifuging the milk and removing fat leaving skimmed milk.

18. (Once Amended) The method of claim 1, wherein the sample has a volume of at least 100 liters.

22. (Once Amended) At least 95%, preferably at least 99%, more preferably at least 99.9% w/w pure human acid a-glucosidase produced by the process of claim 1.

24. (Once Amended) A pharmaceutical composition comprising human acid a-glucosidase as claimed in claim 19.

25. (Once Amended) Human acid a glucosidase of claim 19 for use as a pharmaceutical.

27. (Once Amended) The use of human acid a-glucosidase of claim 19 for the manufacture of a medicament for treatment of human acid a-glucosidase deficiency.

28. (Once Amended) The use of human acid a-glucosidase of claim 19 for the manufacture of a medicament for intravenous administration for the treatment of human acid a-glucosidase deficiency.

32. (Once Amended) A method as claimed in claim 29 being a batch procedure.

33. (Once Amended) A method as claimed in claim 29, wherein

the hydroxylapatite is in the form of a column, optionally the method is a liquid column chromatography procedure.

34. (Once Amended) A method as claimed in claim 29, wherein the heterologous protein is selected from the group consisting of lactoferrin, transferrin, lactalbumin, coagulation factors such as factor VIII and factor IX, growth hormone, a-anti-trypsin, plasma proteins such as serum albumin, C1-esterase inhibitor and fibrinogen, collagen, immunoglobulins, tissue plasminogen activator, interferons, interleukins, peptide hormones, and lysosomal proteins such as a-glucosidase, a-L-iduronidase, iduronate-sulfate sulfatase, hexosaminidase A and B, ganglioside activator protein, arylsulfatase A and B, iduronate sulfatase, heparan N-sulfatase, galactoceramidase, a-galactosylceramidase A, sphingomyelinase, a-fucosidase, a-mannosidase, aspartylglycosamine amide hydrolase, acid lipase, N-acetyl-a-D-glycosamine-6-sulphate sulfatase, a-and ss-galactosidase, ss-glucuronidase, ss-mannosidase, ceramidase, galactocerebrosidase, a-N-acetylgalactosaminidase, and protective protein and others including allelic, cognate or induced variants as well as polypeptide fragments of the same.

35. (Once Amended) A method as claimed in claim 29, wherein the heterologous protein is not one normally found in the milk of an animal.

37. (Once Amended) The method of claim 36, wherein the hydroxylapatite is in the form of a column and the unbound fraction is collected in the flow-through.

BOX MISSING PARTS

Attorney Docket No. 24512-X

A Preliminary Amendment is concurrently filed to removed multiple dependencies from the claims. Examiner is asked to enter this amendment prior to calculating the filing fee.

A Petition for a one month extension of time is submitted with the extension fee of $55.00 attached to this response.

The Commissioner is hereby authorized to charge any deficiency or credit any excess to Deposit Account No. 14-0112.

Respectfully submitted,

NATH & ASSOCIATES PLLC

By: _____

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